

Advanced Blood Management Strategies for Elective Joint Arthroplasty

JODI L. LAYTON, MD; LEE E. RUBIN, MD; JOSEPH D. SWEENEY, MD, FACP, FRCPATH

(NOTE: ALL AUTHORS ARE MEMBERS OF THE MIRIAM HOSPITAL'S TRANSFUSION COMMITTEE.)

ABSTRACT

There is a high prevalence of anemia detected in the preoperative work-up of elective surgical patients preparing for total joint replacement. The impact of anemia in this population has significant implications due to elevations in postoperative morbidity and mortality. By using current clinical guidelines and medical evidence, clinicians can improve outcomes for these patients by employing a three-phase approach, focused on preoperative assessment, intraoperative hemostasis, and postoperative blood product management. Strategies to optimize preoperative hemoglobin levels, reduce intraoperative blood losses, and decrease postoperative transfusion rates can independently and collectively improve overall patient care and surgical outcomes following lower extremity total joint arthroplasty.

KEYWORDS: anemia, total joint arthroplasty (TJA), tranexamic acid (TEA)

INTRODUCTION

Anemia becomes more prevalent as our population ages. Based on World Health Organization (WHO) definitions, the prevalence of anemia will reach approximately 11% in the elderly (age >65 years old). The presence and degree of anemia is affected by comorbidities such as diabetes, cardiovascular disease, renal disease, and other inflammatory conditions. Patients often present to orthopedic surgeries for elective joint arthroplasty at older ages and thus, anemia is a common finding among this population.

Prevalence of Anemia in Elective Orthopedic Surgeries

It is recognized that approximately 40% of patients evaluated prior to elective orthopedic surgeries are found to be anemic by WHO definition (women Hb <12 g/dL, men Hb < 13 g/dL) (WHO, Shander, Saleh).^{11,14,16} Preoperative anemia has been shown to be an independent prognostic factor for increased morbidity and mortality following orthopedic surgery. It is well known that preoperative Hb level is a major predictor of perioperative transfusion rates (Salido).¹⁵ Allogeneic transfusions have been shown to increase hospital length of stay, rate of infections and perioperative mortal-

ity (Salido, Wu, Beattie).^{15,18,1} Some orthopedic surgeries are associated with an anticipated high level of blood loss, thus increasing the possible need for perioperative transfusion. Given the independent risks for morbidity and mortality associated with previously unrecognized preoperative anemia and transfusion rates, guidelines have been developed to address the following areas of need: the preoperative, perioperative, and postoperative periods of patient care.

A standard approach to the detection, evaluation and treatment of anemia in the preoperative period has been identified as an area of unmet need. The Network for the Advancement of Transfusion Alternatives (NATA) developed practice guidelines from a systematic review of the literature. Goodnough, et al. reviewed published literature on the impact of preoperative anemia on clinical outcomes and recommended a standardized approach to detect preoperative anemia. Patients undergoing elective orthopedic surgery should be screened for anemia in order that the underlying cause can be identified and corrected whenever possible.

Preoperative Detection and Management of Anemia

Preadmission testing can occur anytime before a scheduled elective surgery. However, to allow adequate time to detect and correct for anemia, testing should occur as close as possible to 28 days prior to the surgery. For those patients already known to have preexisting anemia, evaluation and treatment should begin as soon as possible.

The most common causes of anemia detected in preoperative testing include iron deficiency anemia, vitamin B12 deficiency, chronic kidney (and associated decreased erythropoietin production), chronic inflammatory diseases, and folate deficiency. As part of the preadmission testing, a complete blood count (CBC) should be drawn and anemic patients identified. Subsequent laboratory tests should screen for the most common etiologies including iron studies, ferritin, vitamin B12, creatinine, and in appropriate patients, folate, thyroid stimulating hormone (TSH), and CRP levels. Algorithms depicting initial and reflexive testing during the work-up of preoperative anemia are available and published (NATA guidelines, Munoz).^{6,10} Treatment of the underlying cause of anemia should then commence to reach to target Hb levels within the normal range (female ≥ 12 g/dL, male ≥ 13 g/dL) within 4-6 weeks by the anticipated time of surgery.

For iron-deficient patients, replacing iron stores with oral versus intravenous iron is somewhat controversial. Overall,

both have been proven to correct iron deficiencies prior to orthopedic surgeries (Beris, Munoz).^{2,10} Oral iron is least costly and easy to administer, however patients often experience gastrointestinal side effects and replenishing iron stores within the limited time frame can be difficult to achieve. Intravenous iron is now available in much safer forms; however, allergic reactions and anaphylaxis are still reported with all formulations. The ease of administration and ability to replenish iron stores during the time frame allotted preoperatively must be balanced with relatively higher costs compared to oral iron.

In the absence of preoperative iron supplementation, postoperative iron repletion has not been shown effective (Munoz, Beris).^{10,2} This is likely due to postoperative healing and inflammatory cytokines altering hepcidin levels thus impairing iron absorption and mobilization in the postoperative period. Postoperative iron supplementation, oral or intravenous, is not recommended.

For patients in whom nutritional deficiencies have been corrected or ruled out, the use of erythropoietin stimulating agents (ESAs) has been shown to decrease perioperative transfusion requirements (Goodnough).⁶ Patients with ferritin values <100 ng/mL or transferrin saturations <20 percent should have iron repletion prior to initiation of ESAs to increase their efficacy. Concurrent iron supplementation with ESAs has also been shown to decrease the dosage of ESAs necessary to correct preoperative anemia.

Anemia should be considered as a treatable symptom of an underlying disease. Preoperative evaluations will sometimes identify more significant comorbidities. If preoperative screening detects evidence of gastrointestinal bleeding, bone marrow disorders or significant renal disease, referrals to specialists such as gastroenterologists, hematologists, or nephrologists may be indicated. A delay in elective surgery may be necessary to insure patient safety and care.

Intraoperative Methods for Reducing Acute Blood Loss Anemia

Attention to meticulous hemostasis has always been paramount during total joint replacement surgery, and remains a crucial element in reducing postoperative anemia. Even when surgeons make a consistent effort to prevent ongoing blood loss via cauterization of peri-articular vessels, there can still be ongoing postoperative bleeding from cut bony surfaces or from bone canals that have been instrumented in the surgery. Efforts to mitigate these “ongoing” blood losses have resulted in improvements in the global understanding and the management of blood loss following arthroplasty surgery.

Two separate meta-analyses, published in 2004 and 2007, both looked at the use of closed suction drainage following orthopaedic surgery in a total of 8959 patients and 9386 surgical wounds. (Parker, Parker)^{12,13} Both reports came to virtually identical conclusions, namely that the use of surgical drains following orthopaedic surgery showed no difference in the rates of wound infection, wound hematoma, or

reoperation rates, but did show significantly increased risk for postoperative blood transfusion. Thus, the routine use of closed suction drains within the intra-articular space following hip and knee arthroplasty has no established clinical benefit for the patient, and now has a strong association with increasing the requirement for postoperative blood transfusion.

More recently, mounting clinical evidence has emerged on the role of using tranexamic acid (TEA) at the time of total joint arthroplasty to reduce the rate of postoperative anemia and transfusion. The pooled risk ratio for needing a transfusion after orthopedic surgery was 0.55 in one review of TEA in 10,488 surgical patients. (Ker)⁸ A second meta-analysis looked more specifically at the use of TEA in total knee arthroplasty, and found that both the amount of blood lost per patient and the number of blood transfusions needed after surgery were significantly less with the use of TEA. (Yang)¹⁹ Importantly, the risks for myocardial infarction, deep vein thrombosis, and pulmonary embolism was not increased in these large series of cases when administering TEA. The ideal TEA dose and route of administration is still under investigation, since it can be given either by injection to the joint immediately following capsular closure in the OR, or via single- or multiple- intravenous injections given in the peri-operative window. (Maniar)⁹

Other methods for intra-operative reductions of blood losses may also prove to be effective, and will be reassessed in the future based on the availability of high-level clinical evidence. For example, the use of neuraxial anesthesia, saline coupled bipolar tissue sealer devices, and the application of topical hemostatic material within the joint are currently under investigation in a number of studies.

Postoperative Tolerance of Normovolemic Anemia and Transfusion Thresholds

The hemoglobin threshold for perioperative transfusion is controversial. Carson et al suggested that symptom-driven transfusion triggers might be an effective blood conserving approach. (Carson 1998)⁴ The Transfusion Requirements in Critical Care (TRICC) trial evaluating clinical outcomes in patients in the critical care setting found that a restrictive transfusion strategy had a non-significant decrease in 30-day mortality; this study did not endorse a restrictive strategy in patients with active cardiac disease. (Hebert)⁷ Given the degree of blood loss expected during elective hip and knee arthroplasty, postoperative transfusion has been commonplace for many decades. Multiple strategies in the preoperative and intra-operative periods aim to reduce postoperative allogeneic transfusion rates. Concern for increased cardiovascular events and impaired quality of life postoperatively has led some to adopt relatively high hemoglobin trigger thresholds for transfusions in “at-risk” patients.

To address these issues, the FOCUS trial (Transfusion Trigger Trial for Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Repair) evaluated higher blood transfusion thresholds (hemoglobin <10 g/dL)

compared with a more restrictive transfusion strategy (hemoglobin < 8 g/dL) on functional recovery, morbidity and mortality in the immediate postoperative period. Carson et al³ concluded that a liberal transfusion strategy did not reduce either the rates of death or inability to walk independently on 60-day follow-up. In this study, there was no appreciable reduction of in-hospital morbidity in elderly patients at high cardiovascular risk following hip fracture surgery using the “restrictive” hemoglobin trigger of 8 g/dL. An additional study focused on quality-of-life measures in the immediate postoperative period after hip or knee arthroplasty, concluding that moderate anemia (across all hemoglobin levels between 8 g/dL to >10 g/dL) was not associated with an impaired functional recovery or a decreased quality of life. (Vuille-Lessard)¹⁷ These more recent studies have led some clinicians and institutions to establish more restrictive transfusion thresholds of asymptomatic anemia to 8 g/dL, even for the elderly or in those patients with underlying cardiovascular risks.

CONCLUSIONS

Preexisting anemia detected prior to surgery, intraoperative blood loss, and postoperative allogeneic transfusion rates have been proven as independent prognostic factors for morbidity and mortality associated with elective orthopedic joint arthroplasty. Blood management strategies to optimize preoperative hemoglobin levels, reduce intraoperative blood losses, and decrease postoperative transfusion rates can independently and collectively improve overall patient care and surgical outcomes following lower extremity total joint arthroplasty.

References

1. Beattie WS, Karkouti K, Wijeyesundrea DN, Tait G. Risk associated with preoperative anemia in noncardiac surgery: a single-center cohort study. *Anesthesiology*. 2009;110:574-81.
2. Beris P, Munoz M, Garcia-Erce JA, Van Der Linden P, et al. Perioperative anaemia management: consensus statement on the role of intravenous iron. *Br J Anaesth*. 2008;100(5):599-604.
3. Carson JL, Terrin ML, Barton FB, et al. A pilot randomized trial comparing symptomatic vs. hemoglobin-level-driven red blood cell transfusions following hip fracture. *Transfusion*. 1998;38:522-9.
4. Carson JL, Terrin ML, Magaziner J, et al. Transfusion trigger trial for functional outcomes in cardiovascular patients undergoing surgical hip fracture repair (FOCUS). *Transfusion*. 2006;46:2192-206.
5. Carson JL, Terrin ML, Noveck H, Sanders DW, Magaziner J, et al. Liberal or restrictive transfusion in high-risk patients after hip surgery. *N Eng J Med*. 2011; 365(26):2453-62.
6. Goodnaugh LT, Maniatis A, Szpalski M, et al. Detection, evaluation, and management of preoperative anaemia in the elective orthopaedic surgical patient: NATA guidelines. *Br J Anaesth*. 2011;106:13-22.
7. Hebert PC, Wells G, Blajchman MA, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. *N Engl J Med*. 1999; 340:409-17.
8. Ker K, Edwards P, Perel P, et al. Effect of tranexamic acid on surgical bleeding: systematic review and cumulative meta-analysis. *BMJ*. 2012;344: e3054 doi: 10.1136/bmj.e3054.
9. Maniar RN, Kumar G, Nayak RM, et al. Most effective regimen of tranexamic acid in knee arthroplasty: A prospective randomized controlled study in 240 patients. *Clin Orthop Relat Res*. 2012;470:2605-12.
10. Munoz M, Garcia-Erce JA, Cuenca J, et al. On the role of iron therapy for reducing allogeneic blood transfusion in orthopaedic surgery. *Blood Transfus*. 2012;10:8-22.
11. Nutritional anaemias. Report of a WHO scientific group. World Health Organization Technical Report Series No. 405. Geneva: World Health Organization, 1968.
12. Parker MJ, Livingstone V, Clifton R, McKee A. Closed suction surgical wound drainage after orthopaedic surgery. *Cochrane Database of Systematic Reviews*. 2007, Issue 3. Art No.:CD001825. DOI: 10.1002/14651858.CD001825.pub2.
13. Parker MJ, Roberts CP, Hay D. Closed suction drainage for hip and knee arthroplasty. A Meta Analysis. *J Bone and Joint Surg Am*. 2004;86-A(6):1146-52.
14. Saleh E, McClelland DBL, Hay A, et al. Prevalence of anaemia before major joint arthroplasty and the potential impact of pre-operative investigation and correction of peri-operative blood transfusions. *Br J Anaesth*. 2007;99: 801-8.
15. Salido JA, Marin LA, Gomez LA, et al. Pre-operative haemoglobin levels and the need for transfusion after prosthetic hip and knee surgery: analysis of predictive factors. *J Bone Joint Surg Am*. 2002;84-A:216-20.
16. Shander A, Knight K, Thurer R, Adamson J, Spence R. Prevalence and outcomes of anemia in surgery: a systematic review of the literature. *Am J Med*. 2004;116:585-69S.
17. Vuille-Lessard E, Boudreault D, Girard F, Ruel M, Chagnon M, Hardy JF. Postoperative anemia does not impede functional outcome and quality of life after hip and knee arthroplasties. *Transfusion*. 2012;52:261-70.
18. Wu WC, Schiffner TL, Henderson WG, et al. Preoperative hematocrit levels and postoperative outcomes in older patients undergoing noncardiac surgery. *JAMA*. 2007;297:2481-8.
19. Yang Z, Chen W, Wu L. Effectiveness and safety of tranexamic acid in reducing blood loss in total knee arthroplasty: A meta-analysis. *J Bone Joint Surg Am*. 2012; 94:1153-9.

Authors

Jodi L. Layton, MD, is affiliated with the Division of Hematology/Oncology, The Miriam Hospital.

Lee E. Rubin is Assistant Professor of Orthopaedic Surgery, Division of Adult Reconstruction, at the Warren Alpert Medical School of Brown University.

Joseph D. Sweeney, MD, is Professor of Pathology and Laboratory Medicine at the Warren Alpert Medical School of Brown University and Director, Coagulation and Transfusion Medicine, Lifespan Academic Medical Center.

Correspondence

Jodi L. Layton, MD
The Miriam Hospital
164 Summit Avenue
Providence RI 02906
401-793-7151
Fax 401-793-7132
jlayton@lifespan.org